PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference WJWFP6532071	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/US2007/011810	International filing date *(day/month/year)* 17.05.2007	Priority date *(day/month/year)* 18.05.2006
International Patent Classification (IPC) or national classification and IPC INV. C07D231/12		
Applicant Arena Pharmaceuticals, Inc.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☒	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
2008-03-14	16.07.2008
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer De Jong, Bart Telephone No. +31 70 340-2833

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US2007/011810

Box No. I Basis of the report

1. With regard to the **language**, this report is based on

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3(a) and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4(a))
   - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-61 as originally filed

   Claims, Numbers

   1-95 as originally filed

   Drawings, Sheets

   1-8 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

5. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 70.2 (e)).

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation to restrict or pay additional fees, the applicant has, within the applicable time limit:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest and, where applicable, the protest fee.

   ☐ paid additional fees under protest but the applicable protest fee was not paid.

   ☐ neither restricted the claims nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-95
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-64,67-95
	No:	Claims	65,66
Industrial applicability (IA)	Yes:	Claims	1-95
	No:	Claims	

2. Citations and explanations (Rule 70.7):

   see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

   and / or

2. Non-written disclosures (Rule 70.9)

   see separate sheet

Reference is made to the following documents:

D1 : WO 2004/058722 A (ARENA PHARM INC) 15 July 2004

D2: WO 2005/012254 A (ARENA PHARM INC) 10 February 2005

Re Item III.

Claims 86-88 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item IV.

Compounds of formula VII according to claim 65 are used as a starting material for the preparation of the compound of formula VI. Compounds of formula VI are however known in the art (see D2, example 1.131).

This is contrary to the requirement that the intermediate and final products should not be separated, in the process leading from one to the other, by an intermediate which is not novel (see PCT Guidelines 10.18).

Therefore, the subject-matter of claim 65 is not so linked with the subject-matter of e.g. claims 1,24,34 as to form a single general inventive concept (Rule 13.1 PCT).

Re Item V.

Novelty

Compounds of formula I, II, V and VII are novel. Therefore the subject-matter of claims 1-95 is novel.

Inventive step

The present application discloses aminophenyl-pyrazoles of formula (I), which are modulators of the 5-HT_{2a} receptor site. Document D1, which is considered to represent the most relevant state of the art, discloses structurally related aminophenyl-pyrazoles having

the same use. The compounds of the present application have a heterocyclyl-ethyloxy group attached to the phenyl group, which is in ortho position of the pyrazole moiety. This is not suggested in the prior art. Therefore compounds of formula (I) and methods for their preparation are inventive. The claimed intermediates of formula II and V benefit from this activity.

Compounds of formula VII (according to claims 65,66) are merely used as a starting material for the preparation of compounds of formula VI, which are known in the art (see document D2, example 1.131). Therefore the compounds of formula VII do not benefit from the inventivity of the compounds of formula (I).

For the subject-matter of claims 65 and 66, document D2 is considered as the closest prior art. In this document a compound of formula VI is prepared starting from aniline precursors. In view of D2, the problem was to provide an alternative method for the preparation of compounds of formula VI and to provide an alternative precursor.

Compounds of formula VI are compounds containing an amide group. A well known method to make amides is the Beckmann rearrangement in which amides are prepared starting from ketones. The ketones are converted to oximes and during the Beckmann rearrangement a new C-N bond is formed.

The skilled person faced with the problem above would consider using the Beckmann rearrangement and would thus come automatically to the precursors which are claimed in claims 65 and 66 of the present application. Therefore, the compounds of formula VII are not considered as inventive.

The argument of the applicant that the skilled person would not consider a precursor that does not have already the C-N bond ignores the fact that the Beckmann rearrangement is a well known method for preparing amides.

Citation of prior art

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D1 is not mentioned in the description.

Industrial applicability

Claims 86-88 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize claims directed to the use of a compound in medical treatment as patentable claims, but may allow claims directed to a product, in particular substances or compositions for use in a first or further medical treatment.